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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,862	06/24/2003	Kenneth Walter Locke	215233-00500	7180

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EXAMINER	
OH, TAYLOR V	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,862	LOCKE ET AL.	
	Examiner	Art Unit	
	Taylor Victor Oh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 June 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The Status of Claims

Claims 1-12 are pending.

Claims 1-12 have been rejected.

DETAILED ACTION

Priority

1. None.

Drawings

2. The drawings filed on 10/30/2001 are objected by the examiner because figs 1, 1a, and 2-6 are generally unclear as to the numbers ,letters, uneven lines ,and labels on the axes.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims 1-7 are directed to a pharmaceutical composition comprising the polymorphic various forms of 4-(6-acetyl-3-(3-(4-acetyl-3-hydroxy-2-propylphenylthio)propoxy)-2-propylphenoxy)butyric acid. According to the specification, there are some remarks about various polymorphic forms of the 4-(6-acetyl-3-(3-(4-acetyl-3-hydroxy-2-propylphenylthio)propoxy)-2-propylphenoxy)butyric acid, but there are no other information about which polymorphic form in the pharmaceutical composition is effective regarding its bioavailability as well as there is no information about the X-ray pattern for Form A in the tablet or capsule in the specification. It is not uncommon to find several polymorphs of compounds existing under normal handling conditions. Every polymorph has its own characteristic X-ray patterns during the pharmaceutical process of making even the final forms such as tablet or capsule containing the active ingredient. Furthermore, many different polymorphs and /or solvates show varying dissolution rates under different conditions : humidity, pressure, temperature, and etc.. Therefore, on the time scale of the pharmaceutical bioavailability, different total amounts of drug are dissolved, resulting in potential bio-inequivalence of the several forms of the drug. Since the above essential aspects are absent in the specification, the skilled artisan in the art is unable to determine which polymorphic form of 4-(6-acetyl-3-(3-(4-acetyl-3-hydroxy-2-propylphenylthio)propoxy)-2-propylphenoxy)butyric acid is suitable for the

pharmaceutical composition with respect to the pharmaceutical bioavailability and the absence of the unique characteristic X-ray pattern for form X in the tablet and capsule form. Therefore, an appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 4, 8, 10, and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 8, and 12, the phrase " other polymorphic forms" is recited. This is vague and indefinite because the skilled artisan in the art may wonder what other forms of polymorphs might have been present in polymorphic Form A. Therefore, an appropriate correction is required.

In claim 3, the phrase " the composition of claim 1, which is in the form of a tablet or capsule " is recited. The expression is vague and indefinite because the composition and the tablet are not the same in their respect functions; the composition can be converted into many different forms of delivery system, whereas the tablet or the capsule is the singular form. Therefore, an appropriate correction is required.

In claims 4, and 5 , the term " Form A" is recited. This expression is vague and indefinite. From the specification, there is no description as to the X-

ray diffraction of Form A after the composition has been converted into the tablet or capsule form , but the Fig 6 only shows 3 possible polymorphs for the compound. Therefore, an appropriate correction is required.

Claims 3, 4, and 7 recite the following limitation:

In claim 3, " a tablet or capsule" in " the form of a tablet or capsule" is recited;

In claim 4 , " the tablet re capsule" in " the tablet of capsule of claim 3 "is recited; and

In claim 7 , " the tablet" in " the tablet of claim 3 "is recited.

There is insufficient antecedent basis for thes limitations in the claims because claim 1 does not disclose any tablet or capsule except the term solid which can not be the representatives for any tablet or capsule. Therefore, an appropriate correction is required.

In claims 4 and 10, the term " substantially" is recited. This is vague and indefinite because the skilled artisan in the art may wonder what is meant by exhibiting PXRD pattern " substantially" ; for example, it may mean that PXRD pattern is substantially clear or the representative PXRD pattern is good enough to be distinguished from other PXRD patterns. Therefore, an appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-5, 8-10, and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated clearly by Ohashi et al (U.S. 4,985, 585).

Ohashi et al discloses 4-(6-acetyl-3-(3-(4-acetyl-3-hydroxy-2-propylphenylthio)propoxy)-2-propylphenoxy)butyric acid crystal compound (see col. 14 , example 33, lines 29-44); the compound is suspended in 5 % solution of Gum Arabic (see col. 17 , lines 41-42) to make its composition. Furthermore, concerning X-ray diffraction patterns and concentration , they are inherently present in the compound and also naturally obtained as unique characteristics for evaluating the compound, not as the novelty of the invention. This composition is identical with the claims.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that

the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohashi et al (U.S. 4,985, 585) in view of Grant et al (Grant & Hack's Chemical Dictionary , 1990 , p. 328).

Ohashi et al discloses 4-(6-acetyl-3-(3-(4-acetyl-3-hydroxy-2-propylphenylthio)propoxy)-2-propylphenoxy)butyric acid crystal compound (see col. 14 , example 33, lines 29-44). In addition, this 4-(6-acetyl-3-(3-(4-acetyl-3-hydroxy-2-propylphenylthio)propoxy)-2-propylphenoxy)butyric acid crystal compound and its composition (see col. 17 , lines 41-42) are useful for prevention and treatment of allergic diseases such as bronchial asthma (see col. 1 ,lines 9-13).

However, the instant invention differs from the prior art in that the claimed composition has at least 90 % of the polymorphic Form A exhibiting the unique PXRD pattern ; the composition is comprised of lactose; the tablet form weighs between 250 and 500 mg.

With respect to the claimed composition having at least 90 % of the polymorphic form A with the unique PXRD pattern, it is not uncommon that the limitation of a process with respect to ranges of pH, time and concentration does not impart patentability to a process when such values are those which would be determined by one of ordinary skill in the art in achieving optimum operation of the process. Concentration is well understood by those of ordinary skill in the art to be a result-effective variable, especially when attempting to control selectivity of a crystallization process. Moreover, it is not uncommon to find several polymorphs of compounds existing under normal handling conditions, just as every polymorph has its own characteristic X-ray patterns. Therefore, there are no patentable weight over these limitations in the absence of unexpected results.

Regarding the tablet form with the weight of from 250 to 500 mg and the composition containing lactose , the reference is silent. However, the reference has offered the indirect guidance as to how much dose a guinea pig can be given; for example, the compound is suspended in 5 % solution of Gum Arabic (see col. 17 , lines 41-42); the dose is in range from 3.125 to 50mg/kg for the pig (see col. 17 ,Table 7). Thus, the amount of the ingredient can be adjusted depending on the needs of the animal.

As for the composition containing lactose, it is well-known in the art that the lactose has been used in the pharmaceutical product for tablet as indicated in Grant et al (page 328). Furthermore, a dry formulation such as tablet form has no patentable weight over a wet formulation. In re Nelson, 97 F.2d 601 (C.C.P.A. 19_). Therefore, it would have been obvious to the skilled artisan in the art to be motivated to adjust the amount of the ingredient as well as the form of the delivery system depending on the needs of the animal.

Ohashi et al expressly teaches the 4-(6-acetyl-3-(3-(4-acetyl-3-hydroxy-2-propylphenylthio)propoxy)-2-propylphenoxy)butyric acid crystal compound (see col. 14 , example 33, lines 29-44) which is useful for prevention and treatment of allergic diseases such as bronchial asthma (see col. 1 ,lines 9-13). Furthermore, it is quite possible that the lactose has been used in pharmaceutical product for tablet as indicated in Grant et al, Therefore, in order to make the tablet form of the desired pharmaceutically acceptable product for preventing and treating bronchial asthma, it would have been obvious to the skilled artisan in the art to be motivated to incorporate the teaching of the Grant et al's lactose into the

Ohashi et al process as an alternative form of the delivery system depending on the needs of the animal. This is because the skilled artisan would expect such a modification to be successful and efficient as shown in the guidance of the Grant et al reference.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T.V.Oh
8/9/04

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